REMARKS

Claims 4, 5, 9-18 and 20 are pending in this application. Claims 1-3, 6-8 and 19 have been canceled herein without prejudice or disclaimer. Claims 4, 5 and 9-18 have been amended.

Claims 4, 5 and 9-18 have been amended to be in independent form, incorporating the limitations of their base claims. The amendments to these claims also include revisions to overcome the rejection under 35 U.S.C. 112, second paragraph, as discussed below.

Regarding Election/Restriction (Office action paragraphs no. 1 and 2)

Non-elected claim 19 has been canceled without prejudice or disclaimer.

Regarding Information Disclosure Statements (Office action paragraphs no. 3-6)

With regard to paragraph no. 5, the Examiner is correct that the Yoshida et al. reference was listed on both previous Information disclosure statements.

In paragraph no. 6, the Examiner indicates that the Suzuki et al. reference (U.S. 5,484,970) does not appear to be particularly relevant. The Examiner is correct that Suzuki et al. '970, entitled "Acoustic insulator", is not relevant. This reference was listed by mistake. An Information Disclosure Statement is filed concurrently with this amendment, listing the intended document.

Claims 1-18 and 20 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action paragraph no. 8)

The rejection is overcome by the amendment to the claims.

The rejection is moot for claims 1-3, 6-8 and 19, which have been canceled herein without prejudice or disclaimer.

Claims 4, 5 and 9-18 have been amended to be in independent form, incorporating the limitations of their base claims. The wording of the claims has also been amended for clarity to overcome the rejection under 35 U.S.C. 112, second paragraph. That is, the wording in the recitation of the base claim, now recited in the amended claims, has been amended as explained below.

The Examiner states that the term "derived from" in claims 1 and 10 is unclear.

The intended meaning of "derived from a prokaryotic cell" in the original claims was that the starting DNA sequence, before the recited modification, is a portion of the DNA sequence from the genome of a prokaryotic cell. This may be understood, for example, by reference to the specification on page 7, line 19, which discusses alteration of a "prokaryotic cell-derived gene". Therefore, in the amendments, the language "derived from a prokaryotic cell" has been replaced by --whose sequence comprises: a portion of the genome of a prokaryotic cell--.

In addition, the word "modified" originally appearing in claim 1, line 4, and claim 10, line 5, has been changed to "altered" in the amended claims. This avoids confusion over the use of words "modified" and "altered", and provides antecedent basis for the term "alteration" in claim 11. Applicants note that the terms "modification" and "alteration" are used interchangeably in the specification.

Claims 1-18 and 20 are rejected under 35 U.S.C. §112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action point 9)

The Examiner refers to the parenthetical expression in claims 1 and 10, in which the letters in NXB are defined. The rejection is overcome by the amendments to the claims as suggested by the Examiner, deleting the parentheses and inserting "wherein" before "N is asparagine".

Claims 1-18 and 20 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action point 10)

The Examiner states that it is unclear if the N-glycosylation referred to in the claims is the N-glycosylation of the entire protein, or N-glycosylation of the specific nNXB site.

The rejection is overcome by the amendments to the claims.

The phrase at issue in original claim 1 was "no N-glycosylation occurs during the expression in a eukaryotic cell." The corresponding phrase has been revised in the amended claims to read: --no N-glycosylation occurs at said NXB site during expression of the DNA molecule in a eukaryotic cell --.

That this was the intended meaning of the original phrase can be seen in the specification on page 6, line 26, which states:

> "the DNA region that is modified so as not to be N-glycosylated is a DNA region that encodes one or more N-glycosylation sites. When a DNA region encoding a plurality of N-glycosylation sites is present in the gene of a prokaryotic cell, **the DNA region encoding the N-glycosylation site that is displayed on the surface may be only modified** considering the conformation of the protein finally obtained, **or all such regions present in said gene may be modified.**" (Emphasis added)

That is, at least one specific region of the DNA molecule encoding an NXB site has been modified so that no N-glycosylation occurs at that particular NXB site. There may be other such specific regions of the DNA that are not modified.

Claims 1-3, 6 and 7 are rejected under 35 U.S.C. §102(a) as being anticipated by Liu et al. (*Prot. Expression and Purification* 19: 304-11(2000)) (of record in the June 2003 IDS). (Office action paragraph no. 12)

The rejection of claims 1-3 and 6-7 is moot in view of the cancellation of these claims without prejudice or disclaimer.

Claim 1-3 are rejected under 35 U.S.C. §102(a) as being anticipated by "Narhi I" (Narhi et al., *Protein Engineering*, 14(2) 135-140 (2001) (Office Action point 13)

The rejection of claims 1-3 is moot in view of the cancellation of these claims without prejudice or disclaimer.

Claims 1-3, 6, 7, 10, 11, 13, 15-18 and 20 are rejected under 35 U.S.C. §103(a) as being unpatentable over the teachings of Jacobson et al. (U.S. Patent No. 5,656,485), or Saitoh et al. (U.S. Patent No. 5,871,742) in view of the teachings of Marini et al. (*Mol. Microbiol.* 38: 552-64), Essex et al. (U.S. Patent No. 6,103,238), and Liu et al. (*Prot. Expression and Purification*, supra), and further in view of the teachings of R. Parekh (*Curr. Opin. Biotech* 2: 730-34) (Office Action point 15)

The rejection of claims 1-3 and 6-7 is moot in view of the cancellation of these claims without prejudice or disclaimer. The rejection of claims 10, 11, 13, 15-18 and 20 is respectfully traversed.

The Examiner cites Jacobson and Saitoh for teaching the use of viruses comprising antigenic proteins to infect eukaryotic cells to express the proteins, and that the antigen may be expressed as a fusion protein with a signal or signal anchor peptide such that the antigen will be secreted or anchored to the cell surface.

The Examiner indicates that it would have therefore been obvious to construct DNAs encoding prokaryotic antigen proteins wherein the antigen is expressed as a fusion with an N-terminal signal peptide.

The Examiner also cites Parekh for teaching that cells have processes for protein N-glycosylation that are not found in eukaryotic cells. This is clearly well known in the art.

The Examiner cites Liu, Essex and Marini for teaching that N-glycosylation may be avoided by modification of NXB sits by substituting another amino acid for Asn.

Applicants note, however, with regard to the Examiner's reference to Jacobson, column 4, lines 7-20, that these lines discuss outer surface expression of an antigen **by bacteria, not by eukaryotic cells**.

Applicants note that prokaryotic immunogenic proteins are naturally produced by prokaryotic cells, and the proteins are not glycosylated and have significant immunogenicity. However, if the prokaryotic immunogenic proteins are produced in eukaryotic cells, sometimes the proteins are glycosylated depending on the kinds of the proteins, and they sometimes exhibit lower

immunogenicity. The present invention is intended to modify prokaryotic immongenic proteins so that when they are expressed in eukaryotic cells, they are not glycosylated and exhibit enhanced immunogenicity.

The Jacobson reference relates to expression of an outer membrane protein in bacterial cells, not expression in eukaryotic cells, and therefore Applicants argue that this disclosure does not suggest the recitation of the present claims.

Moreover, the Essex reference relates to expression of a toxic protein, not an immunogenic protein. Again, this disclosure does not suggest the recitation of the present claims.

Further, claims 15-18 further limit the virus used as the basis of the recombinant virus. In claim 15, this is a poxvirus or a herpesvirus. In claim 16, this is a virus that infects avians. In claim 17, the virus is an avipoxvirus. And in claim 18, the virus is a Marek's disease virus type I, type II or type III. Applicants submit that the Examiner has not provided any specific suggestion or motivation in the references for these claim limitations.

Applicants note that the specific reference showing removal of N-glycosylation sites in a prokaryotic protein, Liu et al., expressed the protein in a specially designed construct in CHO cell lines, for the purpose of making a fusion immunotoxin. Accordingly, there is no suggestion in Liu et al. to use any virus, in particular the ones recited in claims 15-18, as the vector. In fact, it would apparently not make sense for Liu et al. to use a virus as the vector in CHO cells for this purpose, and the recited viruses almost certainly would not work for Liu's purpose.

Applicants therefore submit that the Examiner has not demonstrated a suggestion or motivation in the art for the general modification of prokaryotic genes to remove N-glycosylation

sites in order to make vaccines as in claim 20.

Reconsideration of the rejection of claims 10, 11, 13, 15-18 and 20 is respectfully requested.

Claims 8 and 14 are rejected under 35 U.S.C. §103(a) as being unpatentable over Jacobson, Saitoh, Liu, Essex, Marini, and Parekh as applied to claims 1-3, 6, 7, 10, 11, 13, 15-18 and 20 above, and further in view of Nippon Zeon Co., LTD. (Saito, EP 0905140 - Nippon) Office Action point 16)

The rejection of claim 8 is moot in view of the cancellation of claim 8. The rejection of claim 14 is respectfully traversed.

The Examiner cites EP '140 for teaching that signal sequences from the gB protein of MDV can be used in a fusion protein for the expression of a prokaryotic antigen.

The Examiner's proposed modification of the prior art is based on modification of Saitoh et al. '742, which has as its purpose a vaccine. Although the Examiner has demonstrated that it is known in the art to remove N-glycosylation sites in prokaryotic proteins, **Applicants submit that the Examiner has not actually presented a clear general motivation in the art to do this for the purpose of making vaccines**. Applicants submit that the making of vaccines is the Examiner's proposed motivation which forms the basis for the rejection.

That is, Applicants argue that the Examiner has not provided a suggestion or motivation to both remove N-glycosylation sites in prokaryotic DNA and to create a fusion protein with the recited signal sequences. The Examiner's combination is based on the assumption that one would want to make a particular vaccine, and the Examiner has not clearly demonstrated any general suggestion

or motivation to make a vaccine with such modified prokaryotic DNA.

Reconsideration of the rejection of claim 14 is respectfully requested.

No art rejection is being made over claims 4, 5, 9, or 12 at this time. (Office action paragraph no. 17)

Claims 4, 5, 9 and 12 have been amended to be independent and to overcome the rejections under 35 U.S.C. 112, second paragraph, as discussed above. In addition, claims 5 and 12 have been clarified to refer to SEQ ID NO. 1 or 2, rather than to claim 1 or 2.

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicants undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

ARMSTRONG, KRATZ, QUINTOS, HANSON & BROOKS, LLP

Daniel A. Geselowitz, Ph.D.
Agent for Applicants
Reg. No. 42,573

DAG/plb
Atty. Docket No. **010898**
Suite 1000
1725 K Street, N.W.
Washington, D.C. 20006
(202) 659-2930

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Enclosures: Amendment Transmittal; Petition for extension of time; Information Disclosure Statement w/ PTO-1449 and 1 reference

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